Paper No. 18

UNITED STATES PATENT AND TRADEMARK OFFICE

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BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES

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Ex parte KWAN-MIN J. JEM

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Appeal No. 1999-1425
Application No. 08/393,321

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ON BRIEF

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Before ROBINSON, SCHEINER, and ADAMS, Administrative Patent Judges.

ROBINSON, Administrative Patent Judge.

DECISION ON APPEAL

This is a decision on the appeal under 35 U.S.C. § 134 from the examiner's final rejection of claims 1 - 26, which are all of the claims pending in the application.

Claims 1 and 10 are illustrative of the subject matter on appeal and read as follows:

1. A mechanical method for disruption of plasmid-containing bacterial cells and release of intact plasmid DNA, comprising the steps of:

a) passing liquid suspension of plasmid-containing bacterial cells through an impinging-jet homogenizer with a single interaction chamber at an operating pressure of about 750 to 4,000 psi, whereby the bacterial cells are disrupted and intact plasmid DNA is released, producing a liquid that contains intact plasmid DNA and disrupted bacterial cell debris; and

b) separating the disrupted bacterial cell debris from the liquid containing intact plasmid DNA.

10. A mechanical method for disruption of plasmid-containing bacterial cells and release of intact plasmid DNA, comprising the steps of:

a) passing liquid containing plasmid-containing bacterial cells through a bead mill containing beads of about 0.1 mm to about 1 mm in diameter, at an agitation speed of about 1,000 to 2,500 rpm, wherein the liquid is processed in the bead mill, for a total residence time in the bead mill of at least about 3 minutes, whereby bacterial cells are disrupted and intact plasmid DNA is released; and

b) separating the disrupted bacterial cell debris from the liquid containing intact plasmid DNA.

The references relied upon by the examiner are:

Agerkvist et al. (Agerkvist) "Characterization of *E. Coli*. Cell Disintegrates from a Bead Mill and High Pressure Homogenizers," Biotechnology and Bioengineering, Vol. 36, pp. 1083-1089 (1990)

Sambrook et al.(Sambrook) "Extraction and Purification of Plasmid DNA," Molecular Cloning: A Laboratory Manual, 2nd Edition, Cold Spring Harbor Press Sect 1.21-1.52 (1989)

Sauer et al. (Sauer) Disruption of Native and Recombination *Escherichia Coli* in a High-Pressure Homogenizer," Biotechnology and Bioengineering, Vol. 33, pp. 1330-1342 (1989)

Johnson "Isolation and Purification of Nucleic Acids," Nucleic Acid Techniques in Bacterial Systematics, Stackebrandt et al., eds., John Wiley & Sons, New York, NY., pp. 1-19 (1991)

Grounds of Rejection

Claims 1 - 9 stand rejected under 35 U.S.C. § 103. As evidence of obviousness, the examiner relies on Sambrook and Sauer.

Claims 10 - 26 stand rejected under 35 U.S.C. § 103. As evidence of obviousness, the examiner relies on Sambrook, Johnson, and Agerkvist.

We reverse for reasons set forth herein.

Discussion

In reaching our decision in this appeal, we have given careful consideration to the appellant's specification and claims and to the respective positions articulated by the appellant and the examiner. We make reference to the Examiner's Answer of December 9, 1997 (Paper No. 13) for the examiner's reasoning in support of the rejections and to the appellant's Appeal Brief, filed August 23, 1997 (Paper No. 12), for the appellant's arguments thereagainst.

Background

Applicant describes the claimed invention at pages 6 and 7 of the Specification as being directed to a mechanical method for disrupting plasmid-containing bacterial cells and, thus, releasing the intact plasmid DNA which can then be isolated. One such method comprises the steps of first passing a liquid suspension of plasmid-containing bacterial cells, between one and three times, through an impinging-jet homogenizer with a single interaction chamber at operating pressure of about 750 to 4000 psi, whereby the bacterial cells are disrupted and the intact plasmid DNA is released. Appellant describes a second

method comprising the steps of first passing liquid containing plasmid-containing bacterial cells through a bead mill containing beads of about 0.1 mm to about 1 mm in diameter, at an agitation speed of about 1,000 to 2,500 rpm. Appellant explains that the use of such lower-speed agitation disrupts cells with minimal damage to the DNA plasmids contained therein.

The rejections under 35 U.S.C. § 103

The examiner's rejection of claims 1 - 9 depends on the combined teachings of Sambrook and Sauer.

The examiner relies on Sambrook as describing the isolation of plasmids from host cells using many methods to first disrupt the host cells. (Answer, page 4). The examiner acknowledges that Sambrook does not teach the use of microfluidization disruption as a feasible method for plasmid isolation. (Id.). The examiner cites Sauer as teaching the disrupting of cells using a microfluidizer to isolate intracellular components at 30 - 95 MPa. (Answer, page 5). Therefore, the examiner urges that (Answer, page 4):

> [i]t would have been obvious at the time the invention was made to isolate plasmid DNA from cells using a microfluidizer given that Sauer teaches that microfluidization is a good method for disrupting cells to recover their components.

In rejecting claims under 35 U.S.C. § 103, the examiner bears the initial burden of presenting a prima facie case of obviousness. In re Oetiker, 977 F.2d 1443, 1445, 24 USPQ2d 1443, 1444 (Fed. Cir. 1992). Only if that burden is met, does the burden of

coming forward with evidence or argument shift to the applicants. Id. In order to meet that burden the examiner must provide a reason, based on the prior art, or knowledge generally available in the art as to why it would have been obvious to one of ordinary skill in the art to arrive at the claimed invention. Ashland Oil, Inc. v. Delta Resins & Refractories, Inc., 776 F.2d 281, 297, n.24, 227 USPQ 657, 667, n.24
(Fed. Cir.), cert. denied, 475 U.S. 1017 (1986).

On the record before us, the examiner has not met the initial burden of establishing why the prior art, relied on, would have led one of ordinary skill in this art to arrive at the method of claims 1 - 9. Sambrook, while isolating plasmids from cells by disrupting the cells does not describe any “mechanical” methods of doing so. Sauer, while describing the mechanical disruption of cells using a microfluidizer, is concerned with isolating proteins (page 1330, column 1, first paragraph of the Introduction) and does not suggest that the methodology described would be suitable for use in isolating intact DNA plasmids. Further, we have the statement from Sambrook which suggests that large plasmids are susceptible to damage and should be released from cells by gentle lysis. (Page 1.22, paragraph 1). Thus, in our opinion, the examiner has provided no evidence or facts which could reasonably be read to suggest or direct one of ordinary skill in this art to use the microfluidizer of Sauer in the plasmid isolation process of Sambrook.

In addition, neither reference suggests or describes the use of an operating pressure of 750 to 4,000 psi. While the examiner urges that it would be a matter of routine

experimentation to optimize the disruption of the cells while not damaging the plasmids to be isolated, the examiner has provided no evidence or facts which would guide those of ordinary skill in this optimization process. Before one can optimize a process, there must first be the process. We do not doubt, that the mechanical disruption of Sauer could be applied in some manner to cells to isolate intact plasmids. However, the fact that the prior art could be so modified would not have made the modification obvious unless the prior art suggested the desirability of the modification. In re Gordon, 733 F.2d 900, 902, 221 USPQ 1125, 1127 (Fed. Cir. 1984). In re Fritch, 972 F.2d 1260, 1266, n.14, 23 USPQ2d 1780, 1783-84, n.14 (Fed. Cir. 1982).

In the absence of such evidence, the only suggestion to perform the assay in the manner presently claimed, is provided by appellant's disclosure of the invention. However, use of this information as a basis for establishing a prima facie case of obviousness, within the meaning of 35 U.S.C. § 103, would constitute impermissible hindsight. There must be some reason, suggestion, or motivation found in the prior art whereby a person of ordinary skill in the field of the invention would make the modifications required. That knowledge can not come from the applicants' invention itself. Diversitech Corp. v. Century Steps, Inc., 850 F.2d 675, 678-79, 7 USPQ2d 1315, 1318 (Fed. Cir. 1988); In re Geiger, 815 F.2d 686, 688, 2 USPQ2d 1276, 1278 (Fed. Cir. 1987); Interconnect Planning Corp. v. Feil, 774 F.2d 1132, 1143, 227 USPQ 543, 551 (Fed. Cir. 1985). Since that reason, suggestion or motivation is missing from this record, we can not agree that the examiner

has provided those facts or evidence which would reasonably support a conclusion that the claimed subject matter would have been prima facie obvious within the meaning of 35 U.S.C. § 103. Where the examiner fails to establish a prima facie case, the rejection is improper and will be overturned. In re Fine, 837 F.2d 1071, 1074, 5 USPQ2d 1596, 1598 (Fed. Cir.1988). Therefore, the rejection of claims 1 - 9 under 35 U.S.C. § 103 is reversed.

The examiner's rejection of claims 10 - 26 under 35 U.S.C. § 103 as obvious over the combination of Sambrook, Johnson and Agerkvist is similarly flawed. While relying on Sambrook as discussed supra, the examiner relies on Johnson as teaching the use of a bead mill to disrupt cells, including the use of beads of a size which would appear to correspond, at least to some degree, to that required by the claims. (Answer, page 6). The examiner acknowledges that Johnson "does not teach all of the limitations claimed by appellant." (Id.). However, the examiner urges that "[t]he Johnson procedure could be modified by routine experimentation to produce a method using lower rotation speeds and larger beads." (Id.). While indicating that the use of glass bead disruption "does not fragment DNA to the extent resulting from sonication or passage through a French pressure cell . . . . " (Johnson, page 5, paragraph c), Johnson does not suggest that the technique could be used to isolate "intact DNA plasmids" as presently claimed. Similarly, Agerkvist, in describing Figure 3 states that "the DNA polymer is shear sensitive and will be irreversibly degraded to smaller fragments during the experiment." The examiner offers

no evidence which would reasonably guide one of ordinary skill as to how to modify the methodology of either Johnson or Agerkvist in a manner to arrive at the method of the rejected claims. It is not enough that these methods could be modified, with or without experimentation, to arrive at the claimed invention unless these is something to be found in the prior art which would direct those of ordinary skill in the process. That direction or suggestion is not present on this record. Thus, we conclude that the examiner has failed to provide sufficient evidence to reasonably support a conclusion of obvious within the meaning of 35 U.S.C. § 103 as to the method presently claimed. Therefore, we reverse the rejection of claims 10 - 26 under 35 U.S.C. § 103.

Summary

The rejection of claims 1 - 9 under 35 U.S.C. § 103 as unpatentable over the combined teachings of Sambrook and Sauer is reversed. The rejection of claims 10 - 26 under 35 U.S.C. § 103 over the combined teachings of Sambrook, Johnson, and Agerkvist is reversed.

REVERSED

Douglas W. Robinson Administrative Patent Judge	)
	) BOARD OF PATENT
Toni R. Scheiner Administrative Patent Judge	) APPEALS AND
	) INTERFERENCES
Donald E. Adams Administrative Patent Judge	)

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